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The use of hypnosedative drugs in a university hospital: has anything changed in ten years time?

Annemie Somers^{1*}, Hugo Robays¹, Kurt Audenaert², Georges Van Maele³,
Marc Bogaert⁴, Mirko Petrovic^{4,5}

¹Department of Pharmacy, Ghent University Hospital, ²Department of Psychiatry, Ghent University Hospital, ³Department of Medical Statistics, Ghent University Hospital, ⁴Heymans Institute of Pharmacology, Ghent University, ⁵Department of Geriatrics, Ghent University Hospital

***Corresponding author:**

Annemie Somers

Hospital Pharmacist

Department of Pharmacy, Ghent University Hospital

De Pintelaan 185, 9000 Gent, Belgium

Tel 00-32-9-332.53.73

Fax 00-32-9-332.49.74

E-mail: annemie.somers@uzgent.be

ABSTRACT

Aim: To investigate the use of hypnosedatives (HSs) before and during hospitalisation; to explore the relationship between their use and various demographic and clinical variables; to compare the results with data from a similar study performed in 2000 with particular interest for the adherence to the hospital formulary guidelines.

Methods: Cross-sectional observational survey of 326 hospitalised patients recruited from 10 wards of the Ghent University Hospital, with a patient interview and by evaluation of the medical and nursing files.

Results: In 30.7% of the patients the use of a hypnosedative (HS) before admission was reported. According to the patient interview, 33.1% of the patients used a HS during hospitalisation. But, according to the medical and nursing files, the use of HSs in the hospital was 10% higher (43.3%). In 19.4% of the patients who took HSs before admission, their use was discontinued in the hospital. In 15.6% of the patients who took no HS before admission, a HS was started in the hospital, according to the formulary guidelines (data from files). There was a positive correlation between use of HSs in the hospital and older age, longer hospitalisation, not coming from home, a higher number of HSs taken before hospitalisation, sleeping problems emerging during hospitalisation and CNS disorders respectively. In comparison with the year 2000, we registered a slight decrease in the use of HSs during hospitalisation and a decrease in the number of newly started patients.

Conclusions: The prevalence of HS use in our university hospital is high, mostly as a result of continuation of HSs that were started before admission, as there seems to be no general policy of active cessation. Compared to the survey performed ten years ago, fewer patients are newly started on HSs, and when this is the

case, the formulary guidelines are followed.

Keywords: *Hypnosedatives (HSs), prescribing patterns, formulary guidelines, risk factors*

INTRODUCTION

Hypnosedatives (HSs) are widely prescribed for treatment of insomnia and anxiety, but their long-term use is a reason for concern, because of dependency, side effects, and cost [1-3]. Older patients are especially at risk for impaired cognitive and movement function, with an increased risk of inappropriate sedation, falls and fractures [4-6].

It is well known that the worldwide use of HSs is high, both inside and outside the hospital [7-10]. In Belgium, there is a high prevalence of HSs prescription: surveys conducted in 2001, 2004 and 2008 [11] demonstrated an increasing use of HSs (reported use during the last 2 weeks was 5%, 8% and 9% respectively), and found that the use of HSs increases with age (2004: 17% in patients aged 75 years or more). The Belgian Centre for Pharmacotherapeutic Information in its formulary gives guidance for treatment of acute and chronic insomnia, and advises short term use of benzodiazepines in case non-pharmacological approach is not helpful. However, the choice and dose of benzodiazepines that could be used are not mentioned, and no distinction is made between alprazolam or lorazepam and other benzodiazepines.

In 2000, we registered the use of HSs before and during hospitalisation for 493 patients admitted to ten wards of our hospital. HSs were defined as benzodiazepines and benzodiazepine-like hypnotics (the so called Z-drugs, i.e. zolpidem, zaleplon and zopiclone); we also included two tricyclic antidepressants, i.e. mianserine (ATC N06AX03) and trazodone (ATC N06AX05), as in our hospital, these are only used for HS purposes, as well as the antihistaminic dimetindene (ATC

R06AB03). We found that 29% of these patients took a HS at home and that in 14% of these patients the HS was discontinued during their hospital stay. Furthermore, a HS was prescribed in the hospital in 45.2% of the patients in total and in 28.6% of the 493 patients a HS was started [12]. In view of this high consumption, the hospital formulary guidelines (available upon request) were adapted and distributed throughout the hospital. Briefly, in case of sleeping problems, HSs are not recommended; in case of persisting and debilitating inner tension or adjustment problems, an intermediate-acting hypnosedative is recommended (e.g. lormetazepam or lorazepam), in a low dose and for a short period of time (preferably only once, maximum 1 or 2 weeks). These guidelines were published in the hospital formulary in 2003 and in 2005 as a printed version, which was sent to the medical staff and all head nurses. In 2007, an electronic drug bulletin was distributed with precise recommendations in case a HS is necessary, namely to prescribe lormetazepam 1 mg for a short period of time, and to stop newly started treatment before discharge. It was also stipulated in the drug bulletin that gradual discontinuation of HSs started before hospitalisation should be considered.

We repeated the registration in 2009, to evaluate whether the prevalence and dynamics of HS use was changed. Moreover, we wanted to collect more clinical data, in order to search for risk factors for HSs use which could orient us to more targeted actions.

METHODS

Setting and study design

This prospective, observational, monocentric study was initiated by the Pharmacy and Therapeutic Committee of the Ghent University Hospital, Belgium and

performed on ten hospital wards after approval of the hospital Ethics Committee. The same definition of HSs was used as in the previous study. The ten wards were those where the registration in the year 2000 was performed. The wards included were cardiology, pneumology, nephrology, psychiatry, physical rehabilitation, maternity, head and neck surgery, thoracic and vascular surgery, plastic surgery and abdominal surgery. Five of these wards had the highest and five wards had the lowest consumption of HSs in the year 2000. The method was identical, namely patient interview (after informed consent) by means of a questionnaire, and examination of the medical and nursing files. The interview used in 2009 was almost identical with the one used in 2000. The examination of the medical and nursing files was somewhat altered due to the implementation of electronic prescribing on half of the ten wards. The patients' health problems were also recorded.

We included only patients who stayed at least two nights in the hospital, and interviewed all consecutively admitted patients to the ten hospital wards, during a six weeks period per ward.

Data collection

The use of HSs before and during hospitalisation was measured by means of a patient interview and by examination of the nursing and medical files. The interview took place on a random day during the patient's hospital stay, mostly about a week after admission but this was different depending on the length of stay. Before the interview, the patient was informed about the purpose of the study and was asked for written informed consent.

The patient interview (available upon request) consisted of 18 questions concerning sleeping problems and HS use before and during hospital stay, and

additionally questioned the intended HS use after discharge. The information on HS use was completed with information from the medical and nursing files, done at the moment of patient interview and at the moment of the discharge. In addition, the reason for hospitalisation and the health problems, based on a predefined list of 36 items, were registered. These 36 items were grouped into 9 categories namely cardiovascular, respiratory, gastro-intestinal, metabolic disorders, blood related disorders, infection, malignancy, central nervous system pathology, and orthopaedic and gait disorders. Metabolic disorders mainly concerned diabetes and furthermore acute and chronic renal insufficiency, gout and osteoporosis; central nervous system pathology included amongst others dementia, depression, epilepsy, Parkinson's disease and peripheral neuropathy.

Demographic data that were collected concerned age, gender, origin (home, nursing home, other hospital), and length of stay. The data collection was performed by a hospital pharmacist.

Data analysis

The data were processed in Microsoft Access and transposed to SPSS version 17 for statistical analysis. The influence of age, residence before hospitalisation and previous HS use on sleeping problems and on the number of used HSs before and during hospitalisation was assessed by a Chi-Square Test (Fisher's exact test and linear-by linear association) and by logistic regression. The difference in HS use before, during, and after hospitalisation was analysed by the Friedman test and by the Wilcoxon signed-ranks test. The McNemar test was used for determining the difference between sleeping problems before and during hospitalisation. The influence of age and length of stay on sleeping problems was

assessed by the Mann-Whitney U-test. The Spearman coefficient was used to analyse the correlation between age and length of stay on the one hand and use of HSs on the other hand. Finally, the difference between HS use in the year 2000 and the year 2009 was assessed by a Chi-square test.

RESULTS

Demographics and health problems

During the 2.5 months of the survey, 330 patients were asked to participate; four of them did not accept. The demographic data of the 326 included patients are shown in Table 1. This population consisted of 155 females (47.5%) and 171 males (52.5%). Their mean age was 53.5 years (SD 18.6 years). Twelve patients were transferred from a nursing home, 27 from another hospital, and 287 were living at home before admission. The mean length of hospital stay was 19.1 days (SD 31.8 days, median 9 days). Four of the patients died during their hospital stay.

The distribution of the patients over the ten wards as well as the length of stay per ward is presented in Table 2. During the 6 week survey, around 40 patients were included per ward, except for the rehabilitation and the psychiatry ward, because of longer length of stay and less turn-over of patients as a consequence. In addition, the study duration was shorter for the abdominal surgery ward because of a delay in agreement for participation in the study.

Most of the patients included in the study suffered from cardiovascular disorders (31.0%), followed by metabolic disorders (28.5%), malignancy (15.0%), respiratory disorders (14.1%), gastro-intestinal disorders (9.5%), central nervous system disorders (9.2%), orthopaedic or gait disorders (7.7%), infection (4.9%), or

blood related disorders (2.8%).

Sleeping problems and hypnotic use before admission

The *patient interview* revealed that 131 of the patients (40.2%) suffered from sleeping problems before hospitalisation; out of these 131 patients, 80 (61.1%) took a HS on a regular basis. Out of the 195 patients who did not report sleeping problems before admission, 20 (10.3%) did use a HS, resulting in a total of 100 (30.7%) patients using HSs before admission (Table 3).

The main reasons for HS use mentioned by the patients were a sleep initiation problem (n=68) or a sleep maintenance problem (n=36), as well as nervousness (n=30), fear (n=7) and pain (n=4). Seventeen percent of the patients that took HSs before admission had been given information on future discontinuation of HS use by the treating physician.

According to the *medical and nursing files*, HS were used before admission by 108 patients, with a total of 153 HSs. Thirty-three patients used more than 1 HS before admission (22 patients took 2 HSs, 10 patients took 3 HSs and 1 patient took 4 HSs). The most frequently used HSs were alprazolam (21.3%), lorazepam (18.7%), zolpidem (14.8%) and lorazepam (11.0%).

A Fisher's exact test revealed that females reported more sleeping problems before hospitalisation than males (females 47.1% versus males 33.9%, $p = 0.017$). Suffering from a metabolic disorder was positively correlated with sleeping problems before hospitalisation (metabolic disorder 52.7% versus no metabolic disorder 32.2%, $p = 0.002$). A Mann-Whitney test showed that patients dealing with sleeping problems before admission were significantly older ($p = 0.001$).

Sleeping problems and hypnosedative use during hospitalisation

Concerning sleeping problems in the hospital, 84 patients mentioned a combination of sleep initiation and sleep maintenance troubles (25.8%), 57 patients mentioned sleep maintenance problems (17.5%) and 38 patients mentioned sleep initiation problems (11.7%). In total, 179 patients (or 54.9 % of the study population) had difficulties to sleep in the hospital.

According to the patient interview, 80 patients with sleeping problems, and 28 patients without sleeping problems, took a HS during hospitalisation, resulting in a total of 108 patients or 33.1% of the total study population (Table 3). Ninety of these 108 patients were aware of the brand name.

The main reasons for HS use in the hospital mentioned by the patients, were continuation of HS use before admission (n=51), sleeping problems emerging in the hospital (n=36), worsening of already existing sleeping problems in the hospital (n=7), fear (n=19) and pain (n=6). According to the patient interview, 35 patients were newly started on HSs during hospitalisation (i.e. 15.5% of the patients who did not take a HS before admission). Information about discontinuation of HSs in the future was given by the treating physician to 2 patients that were newly started on HSs during hospitalisation (5.7%).

According to the medical and nursing files, HS use during hospitalisation was found for 141 patients (43.3%), with a total of 235 HSs, although not all HSs were used at the same time (Table 3). For 66 of the 141 patients who took a HS, more than one HS was prescribed (46.8%): 45 patients took 2 HSs, 14 took 3 HSs and for 7 patients 4 HSs were prescribed. Use of more than one HS was more frequent on the psychiatry, thoracic and vascular surgery, rehabilitation, plastic surgery and abdominal surgery wards. For 49 HSs in total, it was not clear whether the drug was

effectively administered, and for 18 patients, the use was only upon request. Only for 83 HSs, a starting and stopping date was found.

According to the patient files, HSs were newly started in a higher percentage of patients were newly started in HSs in comparison to what was reported in the patient interviews, namely 49 (22.5%), but after exclusion of upon request orders without real HS use and after exclusion of a single administration (e.g. before endoscopic procedures), we found that HSs were newly started in 34 patients were newly started on HSs during hospitalisation (15.6%). Most of these patients were admitted at a surgical ward (53.3%), or at the rehabilitation ward (26.7%).

The most frequently HSs prescribed during hospitalisation were lorazepam (32.3%), alprazolam (23.4%), and lorazepam (15.3%). For 18 patients (12.8%), the HS was prescribed upon request and for 83 HSs (35.3%) a starting and stopping date was found.

The linear-by-linear association showed a strong correlation between sleeping problems at home, and the number of used HSs before, during, and after hospitalisation. Sleeping problems emerging in the hospital were correlated with the number of HSs used in the hospital ($p = 0.002$), but not with the number of HSs used before admission ($p = 0.053$). The Spearman correlation test revealed a positive correlation between HS use (before, during and after hospitalisation) and older age ($p < 0.001$), and between HS use during hospitalisation and length of stay ($p < 0.001$). Furthermore, the linear-by-linear association showed a positive correlation between use of HSs in the hospital and not coming from home ($p = 0.032$), a higher number of HSs taken before hospitalisation ($p < 0.001$) and CNS disorders ($p < 0.001$).

The highest prevalence of HS use was found on the rehabilitation, psychiatry,

plastic surgery, thoracic and vascular surgery and cardiology wards. When the patients of the maternity ward are excluded (since there was no use of HSs found), we come to a prevalence of nearly 50% of the patients taking a HS during hospitalisation.

Hypnosedative use after discharge

The patient interviews learned that for 27 patients from the 100 patients who declared to take a HS at home, the HS was stopped during hospitalisation (27.0%). Two of these patients told they wanted to restart the HS, one patient hesitated. For the 73 patients who continued to take the HS in the hospital, 57 patients (76%) told they wanted to continue after discharge, 8 patients (11%) said they wanted to stop, and 8 patients (11%) had not yet decided.

According to the discharge documents, for 21 of the 108 patients who took a HS before admission, the use of HSs was to be discontinued (19.4%), and for 58 patients (17.8%), use of a HS after discharge was envisaged (Table 3). Out of the 21 patients in whom the HS use was stopped, 9 were admitted at a surgical ward and 12 at an internal medicine ward. A linear-by-linear association showed no correlation between sleeping problems in the hospital and intended use of HSs after discharge ($p = 0.73$).

Comparison between 2000 and 2009

The mean and median age of the patients of 2009 was almost the same as in 2000 (mean age: 53.5 years in 2009 and 53.7 in 2000, median age was the same namely 55 years).

The percentage of patients using HSs before hospitalisation was 29.0% in the

year 2000 and 33.1% in 2009, but this difference was non-significant (Chi-square $p = 0.21$). There was a significant decrease in newly started patients (28.6% in 2000 versus 15.6% in 2009; $p < 0.001$), and a borderline significant increase in discontinued patients (14.0% in 2000 versus 19.4% in 2009; $p = 0.055$). Nevertheless, there was no significant decrease in percentage of patients using HSs during hospitalisation (45.2% in 2000 versus 43.3% in 2009; $p = 0.58$), probably due to the higher percentage of patients using HSs before admission, that continued these drugs in the hospital.

DISCUSSION

Strengths and weaknesses

The strength of this study is that the use of HSs before and during, and the intended use after hospitalisation, were recorded accurately, using different sources namely a combination of patient interview, and evaluation of the medical and nursing files. This gave us the opportunity to report highly reliable data about HS use. Furthermore, we searched for risk factors (medical and demographic data), to identify the patients that had the greatest risk of prolonged HS use.

Another strength is the possibility of comparison with the study performed in the year 2000, by using the same patient interview and by including the same hospital wards, which allowed us to evaluate the evolution of HS use.

Our study has several limitations. First of all, the formulary guideline was introduced only passively (by mail and by publication in the formulary), and was perhaps not enough known by the prescribing physicians. It could have been more effective if it would have been implemented in a more proactive way, e.g. by teaching or by prospective advice. Secondly, the wards were selected according to the HS use

in the year 2000, namely five wards with the highest and five wards with the lowest consumption. This means that some wards were excluded, either with routine active cessation or with inappropriate HS therapy (e.g. the geriatric and pneumology ward), which could have biased our results. Therefore, in the future, a hospital wide survey would be more suitable, e.g. when electronic prescribing has been introduced in all hospital wards. Another limitation concerns the data at discharge, since use of HSs after discharge was extracted from the discharge documents, and follow-up of the patient (e.g. by telephone call) was not performed.

Use of HSs before and during hospitalisation

We found a discrepancy between the patient interviews and the medical and nursing files. The lower incidence of HS use reported by the patients could be due to fact that use of a HS as an anxiolytic was not perceived as sleep medication; furthermore some patients, e.g. the severely ill, could not remember properly their medication use, and some HSs were started between the patient interview and the consultation of the patient files. One would expect however that the nursing file would list every administration of drugs during hospitalisation correctly and would therefore be considered as the golden standard considering drug use. However, we noticed that in the nursing and medical files the drugs taken before admission were not always listed correctly (e.g. 'home medications to be continued') and sometimes home medications were kept by the patients themselves (although this is against the agreed procedures). This resulted in loss of information about stopping dates in the patient files, which made correct interpretation of combined HS use very difficult. For instance only for three of the seven patients for whom four HSs were prescribed, we can be sure that the four HSs were combined at the same time. It is therefore likely

that the real use of HSs was somewhere in between 33.1% (reported by the patients) and 43.3% (out of the medical and nursing files).

Notwithstanding the difference between patient interview and file registration, the prevalence of HS use before and during hospitalisation to our hospital is high. In some published studies performed in hospitals, a large variability in HS use, from 15.7% to 45%, was reported [7;8;13-17]. The variability of the results could be due to the characteristics of the population studied, the method for data collection and the duration of the studies. Furthermore, some of these studies were not performed recently, and HS use has probably changed over time.

The comparison of the results from almost ten years ago to those now in the same hospital is probably more meaningful, and learns us that HS use during hospitalisation has not decreased, mostly as a result of continuation of HSs started before admission, as there seems to be no general policy of active cessation. The positive news is that in comparison to ten years ago, a smaller number of patients were newly started on HSs in the hospital, and when this was the case, the formulary guidelines were followed.

Risk factors

We explored the risk factors for HS use during hospitalisation. Since we found that information about discontinuation was provided for only 2 patients who were newly started, we can presume that the risk factors are predictive for prolonged use after discharge.

- Concerning demographic characteristics, HS use in the hospital was significantly higher in older patients, in patients who were not coming from home, and in patients who stayed longer in the hospital. The influence of

age, length of stay and co-morbidities has also been found in previous studies [9;10;15;16].

- As for diagnosis, there was a positive correlation between use of HSs in the hospital and CNS disorders, as well as the intake of a HS before admission.
- With regard to doctors' characteristics, the HS use before admission could not be studied, but we explored more in detail the changes during hospitalisation, and found that relatively more HSs were newly started, and fewer were actively stopped in patients at surgical wards, in comparison with internal medicine wards. However, this should be interpreted with caution since this was a monocentric study in which not all hospital wards were included.

Actions for the future

Our results indicate that older patients who took HSs before admission and who suffer from co-morbidities (especially psychological disorders) are at risk of prolonged HS use and adverse events as a consequence. Future preventive actions must take this population into consideration. We found that 143 of the 162 HS users (88.3%) were not informed by the treating physician about risk of dependence and were not stimulated to reduce HS use. The distribution of formulary guidelines for HS use has been useful for reducing initiation of HSs in the hospital, but another approach is needed for reduction of the high HS use, over the boundaries of the hospital setting.

As mentioned before, there is no general policy of active cessation of HS use in our hospital, and this is probably the same in many other hospitals. The finding that HSs are not often discontinued in the hospital can perhaps be explained by the fact

that hospitalisation in itself leads to anxiety and insomnia. Moreover, abrupt discontinuation is not recommended since this could lead to withdrawal symptoms. Hospitalisation could however be the good moment for drug therapy optimisation, especially for older patients with several co-morbidities [18]. Combined HS use should be discouraged to prevent adverse drug events, and clinicians should focus on short-term use in newly started patients and should inform patients about the need to restrict the use in time. HS use could also be decreased by computer based reminders regarding appropriate use [19]. Furthermore, a tapering scheme could be proposed to the patient, and implemented after the acute phase of illness, through electronic communication between the hospital and the community-based physicians. This could especially be the case for patients admitted to surgical wards, where immediate discontinuation is perhaps not suitable, but where evaluation of appropriate pharmacotherapy is not routinely applied. This action should be facilitated by the government through dissemination of guidelines for HS use and by setting up pilot projects in hospitals.

Several actions have already been taken in our hospital, including automatic stop orders in the electronic prescribing system for newly started HS use, clinical pharmacists' advice to lower HS doses in case patients are sleeping well and to change long-acting substances to intermediate acting HSs (e.g. a clinical pharmacist has been attached to the ward of thoracic vascular and plastic surgery, and more surgical wards should be foreseen for clinical pharmacy in the future). Furthermore, a protocol for active cessation is being set up, using a fast withdrawal scheme over one week, for patients aged more than 55 years suffering from different pathologies [20;21].

CONCLUSION

The prevalence of HS use in our university hospital is high, mostly as a result of continuation of HSs that were started before admission. In comparison to ten years ago, HSs are started in fewer patients in the hospital, and when this is the case, the formulary guidelines are followed. There is still a long way to go to reduce the high consumption of HS, and strategies such as warnings through the electronic prescribing system, clinical pharmacy advice and active tapering and discontinuation schemes for targeted patients should be explored.

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TABLES

Table 1: Demographic data of the participating patients (n=326)

	Females (n = 155)	Males (n = 171)	Total (n = 326)
Mean age (years) \pm SD	49.6 \pm 16.6	57.0 \pm 17.0	53.5 \pm 18.6
Median age (years)	48	62	55
Mean length of stay (days) \pm SD	16.9 \pm 29.2	21.1 \pm 34.0	19.1 \pm 31.8
Median length of stay (days)	8	10	9

Table 2: Number of patients, mean age, median length of stay (LOS) and percentage of HS users per ward during admission (n=326)

	Number of patients	Mean age (years)	Median LOS (days)	% of HS users
Abdominal surgery	17	62.1	13	52.9%
Cardiology	49	67.3	9	53.1%
Head and neck surgery	29	59.8	5	31.0%
Maternity	42	29.9	4	0.0%
Nephrology	42	58.0	9	42.9%
Plastic surgery	28	44.3	13.5	60.7%
Pneumology	43	54.4	8	30.2%
Psychiatry	15	48.5	39	73.3%
Rehabilitation	20	39.6	108	75.0%
Thoracic and vascular surgery	41	62.2	6	56.1%

Table 3: Incidence of HS use: comparison between the year 2000 and 2009

	2000	2009
Total number of patients	493	326
Patients using HSs before admission (interview)	143 (29.0%)	100 (30.7%)
Patients using HSs before admission (file)	N.A.	108 (33.1%)
Patients using HSs in the hospital (interview)	N.A.	108 (33.1%)
Patients using HSs in the hospital (file)	223 (45.2%)	141 (43.3%)
Newly started patients in the hospital (file)	100 (28.6%) (*)	34 (15.5%) (*)
Patients using HSs before admission that were discontinued in the hospital (file)	20 (14.0%) (**)	21 (19.4%) (**)
Patients using HSs after discharge (file)		58 (17.8%)

N.A.: not available

(*) percentage calculated on the number of patients who took no HS before admission

(**) percentage calculated on the number of patients who took a HS before admission

Table 4: Incidence of HS use during hospitalisation, per ward

Ward	patients	HS users	%	>1 HS
Abdominal surgery	17	9	52.9	4
Cardiology	49	26	53.1	7
Head and neck surgery	29	9	31.0	3
Maternity	42	0	0	0
Nephrology	42	18	42.9	6
Plastic surgery	28	17	60.7	9
Pneumology	43	13	30.2	5
Psychiatry	15	11	73.3	9
Rehabilitation	20	15	75.0	9
Thoracic and vascular surgery	41	23	56.1	14
Total	326	141	43.3	66

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